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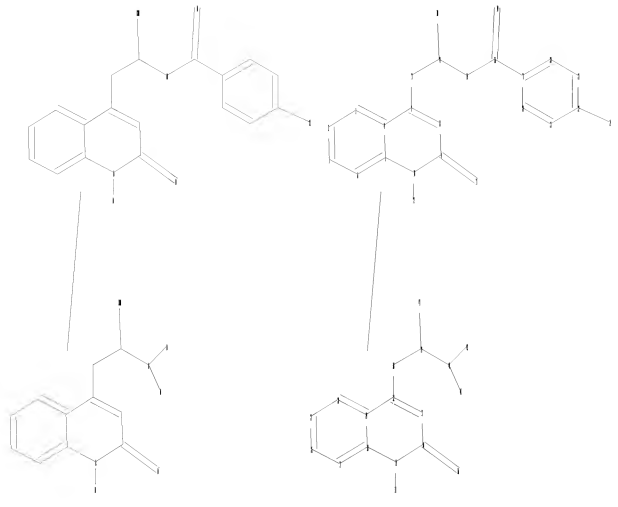
L * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:13:05 ON 30 JUL 2009

=> file reg

=> file casreact

Uploading C:\Program Files\Stnexp\Queries\10587509.str



chain nodes :
11 12 13 14 15 16 18 19 25 36 37 38 39 40 41 42 43
ring nodes :
1 2 3 4 5 6 7 8 9 10 17 20 21 22 23 24 26 27 28 29 30 31 32
33 34 35
chain bonds :
7-13 9-11 10-12 13-14 14-15 14-18 15-16 16-17 16-19 22-25 32-38 34-36
35-37 38-39 39-40 39-41 40-42 40-43
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 17-20 17-24 20-21 21-22
22-23 23-24 26-27 26-31 27-28 28-29 29-30 29-32 30-31 30-35 32-33 33-34
34-35

exact/norm bonds :
4-7 5-10 7-8 8-9 9-10 9-11 14-15 15-16 16-19 29-32 30-35 32-33 33-34 34-35 34-36 39-40
exact bonds :
7-13 10-12 13-14 14-18 16-17 22-25 32-38 35-37 38-39 39-41 40-42 40-43
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 17-20 17-24 20-21 21-22 22-23 23-24 26-27 26-31 27-28 28-29 29-30 30-31

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:CLASS 19:CLASS 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 26

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 08:13:45 FILE 'CASREACT'
SCREENING COMPLETE - 22 REACTIONS TO VERIFY FROM 7 DOCUMENTS

100.0% DONE 22 VERIFIED 7 HIT RXNS 4 DOCS
SEARCH TIME: 00.00.04

L2 4 SEA SSS FUL L1 (7 REACTIONS)

=> d ibib abs hit 1-4

L2 ANSWER 1 OF 4 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:79498 CASREACT
TITLE: Preparation of high-purity 2-(4-chlorobenzoylamino)-3-[2(1H)-quinolinon-4-yl]propionic acid hemihydrate from 2-amino-3-[2(1H)-quinolinon-4-yl]propionic acid
INVENTOR(S): Kawasaki, Kengo; Fukuda, Nobuo; Miyake, Hiroshi; Makio, Shigetoshi
PATENT ASSIGNEE(S): Ohtsuka Pharmaceutical Co., Ltd., Japan

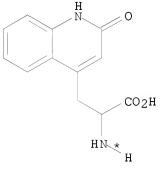
SOURCE: Jpn. Kokai Tokkyo Koho, 15pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

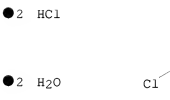
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2008143794	A	20080626	JP 2006-329671	20061206

PRIORITY APPLN. INFO.: JP 2006-329671 20061206

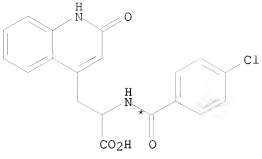
AB 2-(4-Chlorobenzoylamino)-3-[2(1H)-quinolinon-4-yl]propionic acid (I) hemihydrate, useful as a gastrointestinal antiulcer agent (no data), is prepared by amidation of 2-amino-3-[2(1H)-quinolinon-4-yl]propionic acid (II) or its salts with 4-chlorobenzoyl chloride (III), salt formation of the resulting I or I salts with bases in MeOH/H2O, followed by acid treatment. Thus, 608 kg II.2HCl.2H2O was amidated with 437 kg III, treated with 200 L 25% aqueous NaOH solution in 6000 L/400 L MeOH/H2O mixture, and
treated with 1972 L dilute HCl at 65° to give 276 kg I hemihydrate with purity 99.92%.

RX(1) OF 4 A + B ===> C...





A B (1)



● Na

C
YIELD 92%

RX(1) RCT A 914769-50-9

STAGE(1)
RGT D 1310-73-2 NaOH
SOL 7732-18-5 Water

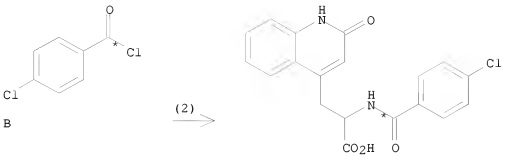
STAGE(2)
RCT B 122-01-0
SOL 67-64-1 Me2CO
CON 15 deg C

STAGE(3)
RGT D 1310-73-2 NaOH
SOL 67-56-1 MeOH, 7732-18-5 Water
CON SUBSTAGE(1) 40 - 50 deg C
SUBSTAGE(2) 50 deg C -> 10 deg C

PRO C 169809-59-0

RX(2) OF 4 A + B ===> H

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



H

RX(2) RCT A 914769-50-9

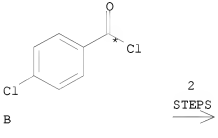
STAGE(1)
RGT D 1310-73-2 NaOH
SOL 7732-18-5 Water

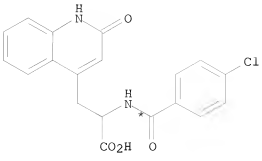
STAGE(2)
RCT B 122-01-0
SOL 67-64-1 Me2CO
CON 15 deg C

PRO H 90098-04-7

RX(4) OF 4 COMPOSED OF RX(1), RX(3)
RX(4) A + B ===> I

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *





●1/2 H_2O

I
YIELD 90%

RX(1) RCT A 914769-50-9

STAGE(1)
RGT D 1310-73-2 NaOH
SOL 7732-18-5 Water

STAGE(2)
RCT B 122-01-0
SOL 67-64-1 Me2CO
CON 15 deg C

STAGE(3)
RGT D 1310-73-2 NaOH
SOL 67-56-1 MeOH, 7732-18-5 Water
CON SUBSTAGE(1) 40 - 50 deg C
SUBSTAGE(2) 50 deg C -> 10 deg C

PRO C 169809-59-0

RX(3) RCT C 169809-59-0

STAGE(1)
RGT D 1310-73-2 NaOH
SOL 7732-18-5 Water
CON room temperature -> 65 deg C

STAGE(2)
RGT J 7647-01-0 HCl
SOL 7732-18-5 Water
CON <30 deg C

PRO I 1033888-72-0

L2 ANSWER 2 OF 4 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 145:27876 CASREACT
TITLE: Catalytic hydrogenolysis process for the removal of the 2-amino-3-[6-bromo-2(1H)-quinolon-4-yl]propionic acid impurity in preparing rebamipide
INVENTOR(S): Nishitani, Shinji; Fukuda, Norio
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

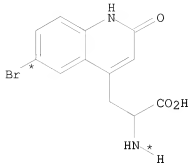
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006059781	A1	20060608	WO 2005-JP22412	20051130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2007503476	T	20070222	JP 2006-546720	20051130
JP 3911008	B2	20070509		
CN 1922145	A	20070228	CN 2005-80005778	20051130
IN 2006DN04286	A	20070803	IN 2006-DN4286	20060725
US 20070249835	A1	20071025	US 2006-587509	20060727
KR 2007085057	A	20070827	KR 2006-715793	20060804

PRIORITY APPLN. INFO.: JP 2004-348425 20041201
WO 2005-JP22412 20051130

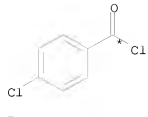
AB In the preparation of rebamipide, the 2-amino-3-[6-bromo-2(1H)-quinolon-4-yl]propionic acid impurity contained in crude 2-amino-3-[2(1H)-quinolon-4-yl]propionic acid is subjected to hydrogenolysis using an aqueous basic solution (e.g., aqueous NaOH) of Raney nickel catalyst and hydrogen to produce pure 2-amino-3-[2(1H)-quinolon-4-yl]propionic acid, which is then amidated with 4-chlorobenzoyl chloride in a basic aqueous solution (e.g., aqueous NaOH) to give rebamipide.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 A + B ===> C

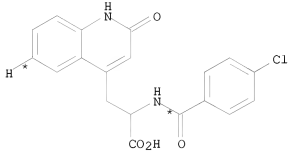


A



B

(1)



C
YIELD 96%

RX(1) RCT A 889573-80-2

STAGE(1)
RGT D 1310-73-2 NaOH
SOL 7732-18-5 Water
CON room temperature

STAGE(2)
RGT E 1333-74-0 H2
CAT 7440-02-0 Ni
SOL 7732-18-5 Water
CON 2 hours, room temperature, 2 atm

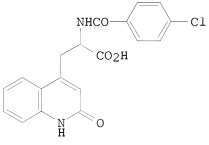
STAGE(3)
RCT B 122-01-0
SOL 67-64-1 Me2CO
CON cooled

STAGE(4)
RGT F 7647-01-0 HCl
SOL 7732-18-5 Water

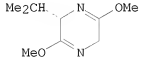
CON acidify

PRO C 90098-04-7

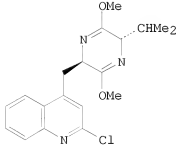
L2 ANSWER 3 OF 4 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 116:128615 CASREACT
TITLE: Synthesis and antiulcer activity of optical isomers of 2-(4-chlorobenzoylamino)-3-[2(1H)-quinolinon-4-yl]propionic acid (rebamipide)
AUTHOR(S): Otsubo, Kenji; Morita, Seiji; Uchida, Minoru; Yamasaki, Katsuya; Kanbe, Toshimi; Shimizu, Takefumi
CORPORATE SOURCE: Tokushima Res. Inst., Otsuka Pharm. Co., Ltd., Tokushima, 771-01, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(11), 2906-9
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



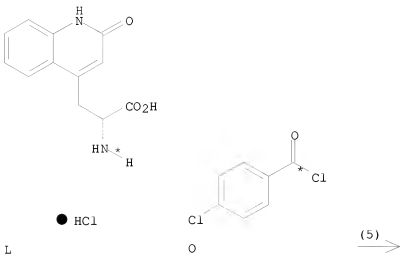
II



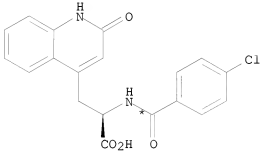
III

AB The enantiomers of rebamipide (I) were prepared and their antiulcer activity was measured against EtOH-induced gastric ulcers. A key step was the condensation of 4-bromomethyl- and 4-chloromethyl-2-chloroquinolines with dimethoxyisopropylpyrazine II to give (pyrazinylmethyl)quinoline III. III was hydrolyzed and acylated with 4-ClC6H4COCl to give (+)-I. (-)-I was prepared analogously.

RX(5) OF 23 ...L + O ===> P



L

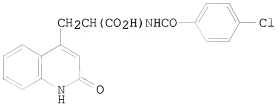


P
YIELD 29%

RX(5) RCT L 137433-09-1, O 122-01-0
RGT Q 584-08-7 K2CO3
PRO P 111911-90-1
SOL 67-64-1 Me2CO, 7732-18-5 Water

L2 ANSWER 4 OF 4 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 105:97287 CASREACT
TITLE: Studies on 2(1H)-quinolinone derivatives as gastric antiulcer active agents. 2-(4-Chlorobenzoylamino)-3-[2(1H)-quinolinon-4-yl]propionic acid and related compounds
AUTHOR(S): Uchida, Minoru; Tabusa, Fujio; Komatsu, Makoto; Morita, Seiji; Kanbe, Toshimi; Nakagawa, Kazuyuki
CORPORATE SOURCE: Tokushima Res. Inst., Otsuka Pharm. Co., Ltd., Tokushima, 771-01, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1985), 33(9),

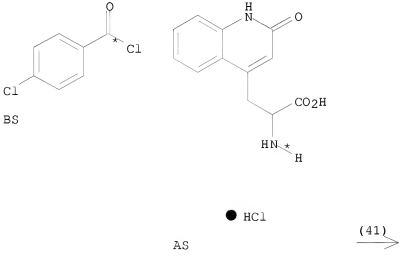
3775-86
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

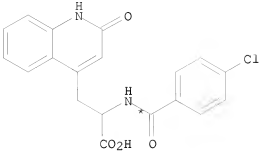


I

AB N-Acyl amino acid analogs of 2(1H)-quinolinone, e.g., I, were prepared and tested for antiulcer activity in rats. These compds. were prepared by acylation of amino acid derivs. of 2(1H)-quinolinone, which were obtained from the reaction of ω-bromoalkyl-2(1H)-quinolinones and acetamidomalonate in the presence of NaOEt, followed by hydrolysis with dilute HCl. I had the most potent activity.

RX(41) OF 219 ...BS + AS ===> BV

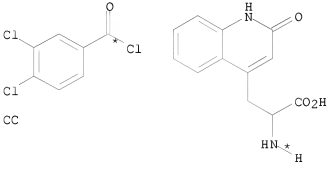




BV

RX(41) RCT BS 122-01-0, AS 4876-14-6
        RGT BM 584-08-7 K2CO3
        PRO BV 90098-04-7
        SOL 67-64-1 Me2CO, 64-17-5 EtOH

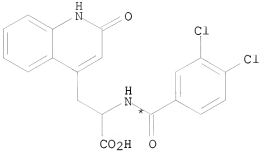
RX(45) OF 219 ...CC + AS ===> CD



CC

● HCl

AS (45) ⟹



CD

RX(45) RCT CC 3024-72-4, AS 4876-14-6
RGT BM 584-08-7 K2CO3
PRO CD 90098-08-1
SOL 67-64-1 Me2CO, 64-17-5 EtOH

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	153.21	153.91

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.12	-3.12

FILE 'STNGUIDE' ENTERED AT 08:15:44 ON 30 JUL 2009
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jul 24, 2009 (20090724/UP).

=> d his

(FILE 'HOME' ENTERED AT 08:13:05 ON 30 JUL 2009)

FILE 'REGISTRY' ENTERED AT 08:13:15 ON 30 JUL 2009

FILE 'CASREACT' ENTERED AT 08:13:21 ON 30 JUL 2009
L1 STRUCTURE UPLOADED
L2 4 S L1 FULL

FILE 'STNGUIDE' ENTERED AT 08:15:44 ON 30 JUL 2009

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 08:25:14 ON 30 JUL 2009